UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,274	10/21/2003	Ramon Eritja	030577	8626

7590 02/06/2008

RAMON ERITJA
VIRIATO 43. 5. 1
BARCELONA, E-08014
SPAIN

EXAMINER	
WOOLWINE, SAMUEL C	
ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
02/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/690,274	ERITJA ET AL.	
	Examiner	Art Unit	
	Samuel Woolwine	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,11,14 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,11,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/ are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status

Claims 10, 11, 14 and 15 are pending in the application.

The rejections under 35 U.S.C. 102 over Soliva et al (NAR 28(22):4531-4539, 15 Nov 2000), US 2006/0008813, and US 2004/0029160, made in OA 03/22/2007 are withdrawn in view of Applicant's amendment submitted 09/26/2007; none of these references teach a triplex made of SEQ ID NO: 6, 7 and 8 or SEQ ID NO: 6, 7 and 9.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10, 11, 14 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10, upon which all other claims depend, requires:

(a) a first oligonucleotide strand comprising at least one 8-aminopurine;

(b) a linker connected to said first strand;

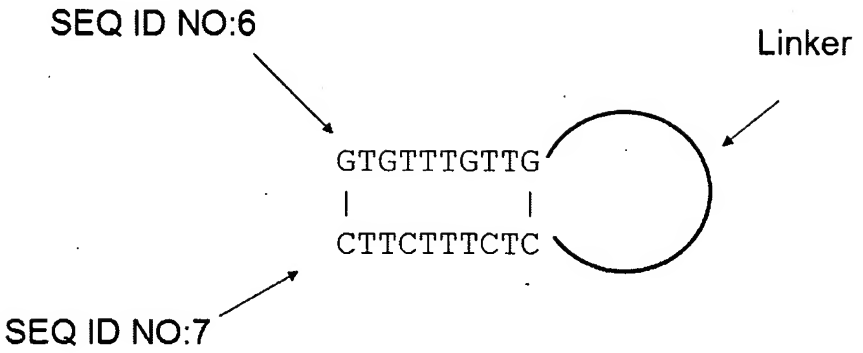
(c) a second oligonucleotide strand connected to the opposite end of said linker from the first oligonucleotide strand and capable of forming a hairpin with said first oligonucleotide strand; and

(d) a third oligonucleotide comprising pyrimidines, where said third oligonucleotide is substantially complementary to and antiparallel to said first oligonucleotide strand.

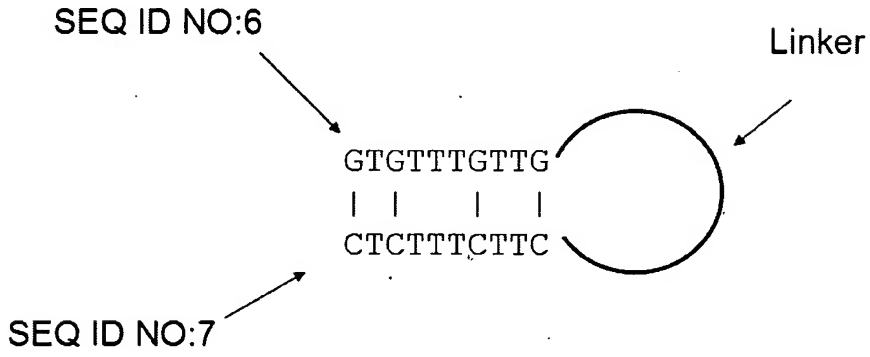
Then claim 10, as amended, goes on to require that the triplex is selected from one formed from SEQ ID NO: 6, 7 and 8 or one formed from SEQ ID NO: 6, 7 and 9, referring to SEQ ID NO: 6 as "first oligonucleotide", SEQ ID NO: 7 as "second oligonucleotide" and SEQ ID NO: 8 or 9 as "third oligonucleotide". Applicant points to Table 2, page 28 of the specification as filed for support for the amendment. However, as seen in Table 1, page 27 of the specification as filed (which actually shows the sequences of SEQ ID NO: 6, 7, 8 and 9), there are inconsistencies within the claim.

Firstly, SEQ ID NO: 8 and 9 (referred to in the claim as "third oligonucleotide") do not comprise pyrimidines (they comprise only adenine or guanine bases, which are purines; pyrimidines would be Cs and Ts, not As and Gs). Secondly, SEQ ID NO: 6 (referred to in the claim as "first oligonucleotide") does not comprise at least one 8-aminopurine. Only SEQ ID NO: 9 is shown in Table 1 to comprise an 8-aminopurine (A^N=8-aminoadenine; see specification as filed, page 9, first paragraph under Free energy calculations for explanation of the symbol A^N seen in SEQ ID NO: 9 of Table 1). Therefore, even if one were to rearrange the designation of "first", "second" and "third" in the claim, a triplex formed from SEQ ID NO: 6, 7 and 8 does not comprise an 8-aminopurine as required by the claim. The sequence listing supplied with the instant application was checked to confirm that only SEQ ID NO: 9 comprises an 8-aminopurine.

Additionally, SEQ ID NO: 6 and 7 (referred to in the claim as "first" and "second" oligonucleotide) if connected by a linker, would look like this:



or, if joined in the other orientation (e.g. 3'-3'), like this:



In either case, it does not appear as though the "first" and "second" oligonucleotides would be capable of forming a hairpin.

It would appear that only SEQ ID NO: 9 can be the "first" oligonucleotide, and that it must be connected to either SEQ ID NO: 6 or 7 via a linker in either a parallel or antiparallel fashion (the disclosure indicates the possibility of G-G and A-A pairing in the formation of a helix, so either SEQ ID NO: 6 or 7 could presumably be the "second"

oligonucleotide). Likewise, since both SEQ ID NO: 6 or 7 comprise pyrimidines (Ts), either could presumably be the "third" oligonucleotide.

Because the examiner cannot make a reasonable interpretation of the claim, as the structure of the claimed compound cannot be discerned in view of the conflicting claim requirements, no search over the prior art is possible. See MPEP 2143.03(I):

"Compare *In re Wilson*, 424 F.2d 1382, 165 USPQ 494 (CCPA 1970) (if no reasonably definite meaning can be ascribed to certain claim language, the claim is indefinite, not obvious) and *In re Steele*, 305 F.2d 859,134 USPQ 292 (CCPA 1962) (it is improper to rely on speculative assumptions regarding the meaning of a claim and then base a rejection under 35 U.S.C. 103 on these assumptions)."

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10, 11, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment to claim 10 is not supported in the original disclosure.

Applicant points to Table 2 (page 28) for support. While Table 2 (as well as Table 1, page 27) discloses the use of SEQ ID NO: 6, 7 and 8 and SEQ ID NO: 6, 7 and

9 to form a helix, there is no disclosure of any linker joining any two of these sequences. In fact, Tables 1 and 2 appear to describe simulations (see page 7 of specification as filed, Molecular dynamics simulations). Although Applicant generally contemplates a linker joining an oligonucleotide comprising an 8-aminopuring to another oligonucleotide carrying GT or GA sequences (see page 1, paragraph entitled Field of the Invention), this does not provide support for the specific combination of SEQ ID NO: 9 joined via a linker to SEQ ID NO: 6 or 7. It is noted that Applicant's specification does illustrate "two" oligonucleotides joined by a T_4 linker (e.g. SEQ ID NO: 16, page 33) in a triplex with another "third" oligonucleotide (SEQ ID NO: 15, page 33). Thus, Applicant's specific designation of a "first" and "second" oligonucleotide (joined via a linker) with its own single SEQ ID NO would seem to indicate that, had Applicant contemplated SEQ ID NOS 9 and 6 (or 9 and 7) joined with a linker, there would have been a single SEQ ID NO designated for this as well.

This is a NEW MATTER rejection.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 10, 11, 14 and 15 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

As stated at MPEP 2107 (Guidelines for Examination of Applications for Compliance with the Utility Requirement), the first question to be addressed is whether the claimed invention has a well-established utility; see MPEP 2107(II)(A)(3), which reads in part:

> An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible.

In the instant case, the only utility that would seem to be served by the claimed invention, beyond those utilities asserted by Applicant (see below), would be the use of the claimed invention as a research tool to study the behavior and properties of nucleic acid hybridization and triplex formation. This use appears to account for the bulk of the specification. However, this cannot be considered a *substantial* utility (or thus, a well-established utility), because as set forth at MPEP 2701.01(I)(B):

> *>"[A]n application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the 'substantial' utility requirement, an asserted use must show that the claimed invention has a significant and presently available benefit to the public." *Fisher*, 421 F.3d at 1371, 76 USPQ2d at 1230. The claims at issue in Fisher were directed to expressed sequence tags (ESTs), which are short nucleotide sequences that can be used to discover what genes and downstream proteins are expressed in a cell. The court held that "the claimed ESTs can be used only to gain further information about the underlying genes and the proteins encoded for by those genes. The claimed ESTs themselves are not an end of [applicant's] research effort, but only tools to be used along the way in the search for a practical utility... [Applicant] does not identify the function for the underlying protein-encoding genes. Absent such identification, we hold that the claimed ESTs have not been researched and understood to the point of providing an immediate, well-defined, real world benefit to the public meriting the grant of a patent." Id. at 1376, 76 USPQ2d at 1233-34). Thus a< "substantial utility" defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, both a therapeutic method of treating a known or newly discovered disease and an assay method for identifying compounds that themselves have a "substantial utility" define a "real world" context of use. An assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring. On the other hand, the following are examples

> of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities":
>
> (A) Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved;
>
> (B) A method of treating an unspecified disease or condition;
>
> (C) A method of assaying for or identifying a material that itself has no specific and/or substantial utility;
>
> (D) A method of making a material that itself has no specific, substantial, and credible utility; and
>
> (E) A claim to an intermediate product for use in making a final product that has no specific, substantial and credible utility.

The utility discussed above would fall under category (A), and thus does not constitute a substantial utility.

The next question to consider is whether Applicant has asserted any utilities that are specific, substantial, and credible. Consulting the specification, the following asserted utilities were found (page 2):

"For example, triple helices are used for the extraction and purification of specific nucleotide sequences, control of gene expression, mapping genomic DNA, detection of mutations of homopurine DNA sequences, site-directed mutagenesis, triplex-mediated inhibition of viral DNA integration, nonenzymatic ligation of double-helical DNA and quantitation of polymerase chain [reaction ?]."

While these utilities are deemed credible, they fail the "specific and substantial" test. All of these asserted utilities would seem to operate in a sequence-specific manner. In other words, a triplex of sequences A, B and C would, for example, be useful for purifying one nucleotide sequence, while a triplex of sequences D, E and F

would be useful for purifying a different nucleotide sequence. Thus the analysis hinges on whether there is any specific and substantial utility served by the triplex of SEQ ID NO: 6, 7 and 8 (or 9).

With regard to the "extraction and purification of specific nucleotide sequences", "site directed mutagenesis" and "nonenzymatic ligation of double-helical DNA", these asserted utilities are not a substantial utility, as they would fall within category (D) above. Applicant has not disclosed any particular utility for the specific nucleic acid sequence that could be extract and purified, or manufactured by mutagenesis or nonenzymatic ligation, using the claimed triplex.

With regard to the "mapping genomic DNA", "detection of mutations of homopurine DNA sequences", and "quantitation of polymerase chain [reaction ?]" utilities, these would fall within category (C) above. Applicant has not disclosed any particular utility for the specific nucleic acid or mutation that could be detected or quantitated by the claimed triplexes. Also note that MPEP 2107.01(I)(A) states:

> Similarly, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. >See *In re Fisher*, 421 F.3d at 1374, 76 USPQ2d at 1232 ("Any EST [expressed sequence tag] transcribed from any gene in the maize genome has the potential to perform any one of the alleged uses... Nothing about [applicant's] seven alleged uses set the five claimed ESTs apart from the more than 32,000 ESTs disclosed in the [ ] application or indeed from any EST derived from any organism. Accordingly, we conclude that [applicant] has only disclosed general uses for its claimed ESTs, not specific ones that satisfy § 101.").<

Thus, not only are these utilities not substantial, they are also not specific.

Finally, the "control or gene expression" and "inhibition of viral DNA integration" utilities, Applicant has not disclosed any specific gene whose expression could be controlled by the claimed triplex, or why controlling expression of that gene would be

useful. Applicant has not disclosed any particular virus whose integration could be inhibited by the claimed triplex. Consequently, these utilities fall within category (B) above.

Based on the finding that none of the asserted utilities for the claimed triplex constitute a specific and substantial utility, claims 10, 11, 14 and 15 do not comply with the utility requirement under 35 U.S.C. 101.

Claims 10, 11, 14 and 15 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Woolwine whose telephone number is (571) 272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

scw

/Young J. Kim/
Primary Examiner
Art Unit 1637
Technology Center 1600